UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/901,812	07/10/2001	Diane Pennica	GENENT.083A	7879

9157 7590 02/24/2004

GENENTECH, INC.
1 DNA WAY
SOUTH SAN FRANCISCO, CA 94080

EXAMINER	
RAWLINGS, STEPHEN L	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 02/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/901,812	PENNICA ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-66* is/are pending in the application.

4a) Of the above claim(s) *7 and 11-66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-66* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20011203, 20020820*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The election with traverse filed November 11, 2003 is acknowledged and has been entered. Applicants have elected the invention of group 45 as set forth in the restriction of the Office action mailed October 3, 2003.

2. Claims 1-66 are pending in the application. Claims 7 and 11-66 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the paper filed November 11, 2003.

3. Claims 1-6 and 8-10, insofar as the claims are drawn a method for the selective enhancement of the expression of Stra6 in a tumor cell comprising treating the tumor cell with a retinoid, wherein said tumor cell is a breast cancer or colon cancer cell, are currently under prosecution.

Election/Restrictions

4. Applicant's traversal of the restriction and election requirement set forth in the Office action mailed October 3, 2003 is acknowledged. Applicant has traversed the restriction arguing that restriction is improper if the restricted inventions can be searched without serious burden, because the search required to examine different inventions involves searching the same class and subclass. Applicant has further argued the search of the elected group is likely to identify art pertaining to the other groups.

Applicants' grounds of traversal have been carefully considered but not found persuasive. The inventions are distinct for the reasons set forth in the Office action mailed October 3, 2003. Classification is but one indication of the burden of search; and in the art of cancer immunotherapy, the extent of the required literature search is the better indication of the burden of search. Because the search that would be required to examine any one invention is not co-extensive with the search that would be

required to examine any other, a different search would need be performed to examine any other, which need would constitute serious burden. Accordingly, at first glance the restriction is proper.

In reply to Applicant's argument the search of the elected group is likely to identify art pertaining to the other groups, if prior art, which anticipates or renders any other invention obvious, should be found in the process of searching the elected invention, rejoinder is proper. In this instance, the search of the elected invention revealed prior art anticipating the invention of group 44, claims 1-10, insofar as the claims are drawn to a method for selectively enhancing the expression of Stra6 in a colon cancer cell. Accordingly, group 44 has been rejoined to the elected invention of group 45.

For the above reasons, the remainder of the restriction and election requirement set forth in the Office action mailed October 3, 2003 is deemed proper and is therefore made FINAL.

Priority

5. Applicants' claim to the benefit of the earlier filing dates of US Provisional Application No. 60/228,914, which was filed August 29, 2000, and US Application No. 09/759,056, which was filed January 21, 2001, is acknowledged. However, at page 1 of the present specification it is disclosed that US Application No. 09/759,056 claims priority to US Provisional Application No. 60/175,849, which was filed January 13, 2000. Accordingly, the pendency of US Provisional Application No. 60/175,849 had expired before US Application No. 09/759,056 was filed. As such, this application is not given benefit is the filing date of US Provisional Application No. 60/175,849. Nevertheless, according to the disclosure at page of the present specification US Application No. 09/759,056 also claims priority to US Provisional Application Nos. 60/197,089 and 60/228,914, which were filed April 14, 2000 and August 29, 2000, respectively, so the earliest effective filing date of this application is deemed April 14, 2000.

Declaration

6. The declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration filed December 26, 2001 is defective because it does not state the inventive entity has reviewed and understands the contents of the specification, *including the claims*.

Specification

7. The specification is objected to because the use of numerous improperly demarcated trademarks has been noted in this application. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

Examples of improperly demarcated trademarks include Taxol™ (page 19), TaqMan™ (pages 25 and 61), American Type Culture Collection™ (pages 47 and 80), Qiagen (page 52), AmpliTaq™ (page 62), RNeasy™ (page 63), Effectene (page 73), and Affymetrix™ Mouse Gene Chip™ (page 74).

Appropriate corrections are required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at http://www.uspto.gov/web/menu/search.html.

8. The specification is objected to because of the following informality: "Qiagen" is misspelled at page 54, line 6.

Claim Objections

9. Claims 5, 6, and 10 are objected to because the claims are drawn in the alternative to the subject matter of non-elected inventions. Appropriate action is required.

Claim Rejections – 35 USC § 112

10. Claims 1-6 and 8-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-6 and 8-10 are drawn to a method for selectively enhancing the expression of Stra6 in a tumor cell characterized by aberrant Wnt signaling comprising treating said cell with a retinoid, wherein said retinoid is retinoic acid and said tumor cell is a human breast cancer cell.

In the paragraph bridging pages 13 and 14, the specification catalogs some known members of the Wnt signaling pathway. At page 14, the specification defines the term "characterized by aberrant Wnt signaling" as including "genetic defects and/or altered expression patterns (including mutations, amplification, over-expression and/or suppression) of any of these members of the Wnt signaling pathway, or any other members, known today **or hereinafter identified**" (emphasis added) (lines 9-11).

Accordingly, the claims encompass a method comprising treating a tumor cell characterized as having genetic defects and/or altered expression patterns, including mutations, amplification, over-expression, and/or suppression of any known, *or yet to be discovered* member of a genus of proteins involved in a Wnt signaling pathway. As the disclosed or known members of the Wnt signaling pathway are disparate in structure and function, the skilled artisan cannot envision, or even predict the structure of any hereinafter identified members of Wnt signaling pathway. As members of the Wnt signaling pathway have yet to be discovered, the members of the genus of tumor cells having aberrant Wnt signaling cannot be recognized or distinguished from others. Moreover, apart from the tumor cells described in the specification as having aberrant

Wnt signaling the skilled artisan cannot envision or predict the nature of the genetic defects and/or altered expression patterns, including mutations, amplification, over-expression, and/or suppression of the known members of the Wnt signaling pathway, so as to immediately recognize any other tumor cells having aberrant Wnt signaling.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016.

Even given the benefit of Applicant's disclosure, the skilled artisan could not immediately recognize a tumor cell have aberrant Wnt signaling as defined at page 14 of the specification, apart from the tumor cells described in the specification as having aberrant Wnt signaling. According, the disclosure would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the invention was made. Therefore, the disclosure is insufficient to meet the written description requirement set forth under 35 USC § 112, first paragraph.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 is indefinite because the claim recites, "wherein said protein is over-expressed in tumor cells relative to corresponding normal cells". The recitation of term "corresponding" renders the claim indefinite because it cannot be ascertained how the claim requires the normal cells to correspond to the tumor cells. For example, it cannot be ascertained whether the normal cells must be of the same tissue origin, or alternatively of the same cell type. Because of apparent ambiguity, the metes and bounds of the invention are not clearly and particularly delineated to meet the requirements set forth under 35 USC § 112, second paragraph.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

14. Claims 1-6 and 8-10 are rejected under 35 U.S.C. 102(a) as being anticipated by Chu et al. (*J. Nutr.* **129**: 1846-1854, 1999), as evidenced by Pennica et al. (*Proc. Natl. Acad. Sci. USA.* **95**: 14717-14722, 1998) and Szeto et al. (*Cancer Res.* **61**: 4197-4205, 2001; cited by Applicant).

Claims 1-6 and 8-10 are drawn to a method for selectively enhancing the expression of Stra6 in a tumor cell characterized by aberrant Wnt signaling comprising treating said cell with a retinoid.

In Table 2 at page 1851, for example, Chu et al. teaches the effects of treating human breast and colon cancer cells with an amount of retinoic acid effective to alter the expression the cancer cells' genes.

Chu et al. does not explicitly teach the cancer cells treated with retinoic acid are characterized by aberrant Wnt signaling. Nonetheless, as evidenced by the teachings

of Pennica et al., the human colon cancer cell of Chu et al. is characterized by aberrant Wnt signaling. In the paragraph bridging pages 13 and 14, the specification catalogs some known members of the Wnt signaling pathway, including the WISP genes. At page 14, the specification defines the term "characterized by aberrant Wnt signaling" as including "genetic defects and/or altered expression patterns (including mutations, amplification, over-expression and/or suppression) of any of these members of the Wnt signaling pathway, or any other members, known today or hereinafter identified" (lines 9-11). In Figure 5 at page 14720, for example, Pennica et al. teaches the WISP genes of the human colon cancer cell of Chu et al. are amplified and over-expressed.

Chu et al. does not explicitly teach the selective enhancement of the expression of Stra6 in the cancer cells treated with retinoic acid; nor does Chu et al. expressly teach the capability of Wnt-1 and retinoic acid to synergistically enhance the expression of Stra6, nor the over-expression of Stra6 in the cancer cells relative to corresponding normal cells. Nonetheless, as evidenced by the teachings of Szeto et al., Stra6 was previously known to be up-regulated by retinoic acid; accordingly, the treatment described by Chu et al. results in the selective enhancement of Stra6 expression in the tumor cells. In addition, Szeto et al. demonstrates the capability of Wnt-1 and retinoic acid to synergistically enhance the expression of Stra6 in tumor cells, and as further evidenced by the teachings of Szeto et al., Stra6 is over-expressed in tumor cells relative to corresponding normal cells.

Conclusion

15. No claims are allowed.

16. The prior art made of record and not relied upon is considered pertinent to Applicants' disclosure. Bouillet et al. (*Mech. Dev.* **63**: 173-186, 1997; cited by Applicant) teaches *Stra6* is a retinoic acid-inducible gene. Smolich et al. (*Dev. Biol.* **166**: 300-310, 1994) teaches the coordinate regulation of gene expression by Wnt-1 and retinoic acid in the P19 embryonal carcinoma cell line. US Patent No. 5,891,866 A teaches a

method for inhibiting the proliferation of breast cancer cells comprising treating the cells with retinoic acid.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne (Bonnie) Eyler, Ph.D. can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
February 11, 2004

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600